

## THE IMMEDIATE ANTECEDENTS OF SUDDEN DEATH

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### ABSTRACT

*A 5 yr prospective survey of 1839 coronary heart disease (CHD) deaths, in 260.000 employed men aged 20–65 – and a detailed study of 142 deaths of all causes in 1020 men aged 40–65 who were observed for 5 yrs with repeated examinations and 24 hr ECG recordings shows the following:*

*60.4% of CHD deaths were «sudden» (SD) in <1 hr; 42.5% of SDs were in men not previously known to have heart disease. The cardiac phenomena of all deaths could be classified as «arrhythmic» (ARD) or «circulatory failure» (CFD). 91% of SDs in <1 hr and 85% of SDs in <24 hrs were ARDs. ARDs and CFDs occurred under different conditions with different precipitating causes and different predictive «risk factors».*

*At time of death 85% of ARDs were asleep, 88% awake and 42% active. 92.5% had myocardial disease: occlusions of major coronary vessels, scarring or fibrosis; recent acute MI or CO; hypertrophy  $\geq 400$  gms 80%; congestive heart failure 45%; cardiac dilatation 23%. 25% had severe anemia or anoxemia. 85% had major chronic disorders of rhythm or conduction (VPCs  $\geq 10/1000$  36%; pairs of PVC 15%;*

*EC VPCs 23%; QRS  $\geq 11$  sec 28 %).*

*At time of death 100% of CFDs were comatose and not arousable. 48% had no clinical evidence of heart disease. 57% had myocardial disease: definite CHD 26%; hypertrophy  $\geq 400$  gms 47%; chronic CHF 29%; cardiac dilatation 13%. 27% had major disorders of rhythm or conduction (VPC  $\geq 10/1000$  20%; pairs of PVC 10%; EC VPCs none; QRS  $\geq 11$  sec 10%).*

*ARDs were precipitated by activities known to be associated with vagal effects on heart in 17.1% of the men; by activities known to be associated with sympathetic effects of heart in 34.1%, episodes of acute myocardial ischemia in 14.6%; or occurred during no apparent precipitating event in 34.1%. CFDs were precipitated by hemorrhage, trauma, infection, stroke, or other cause of peripheral vascular failure (87%), and by myocardial failure (13%).*

*Risk factors at age 55 for ARD in 5 years are confounded and interact. Men with combinations have higher risk. A risk factor for CFD is the presence of potentially fatal non-cardiac disease likely to cause coma or peripheral vascular collapse.*

The purposes of our investigations have been to ascertain the conditions under which sudden deaths occur among middle-aged American men, the events that precipitate these deaths, and the factors that determine the risk of sudden death within five years.

METHODS

The investigations have been based on a five year prospective survey of 1839 deaths attributed to coronary heart disease among 269,755 men aged 20–65 employed in the telephone industry throughout the continental United States (1), and on 1020 five year intensive prospective observations of men aged 40–65, with repeated (1–7 times) comprehensive medical histories and examinations; reviews of activities, medications, smoking, drinking, and time budgets; blood lipids, glucose tolerance, serum uric acid, and biochemical and hematological profiles; chest x-rays; 12-lead ECG's; and 24 hour recordings of ECG's; plus investigations of all deaths (total 142) that occurred (2). The subjects, from 21 white and blue collar industries and two labor unions in New York, New Jersey and Connecticut, included 333 selected from medical records because of features thought to indicate «high risk», and 687 designated in random samples from age cohorts of employed men in which the sudden death rates and the incidence of coronary heart disease were determined to be similar to those of comparable men nationwide. The prevalence of CHD, hypertension, body build, smoking, drinking, serum cholesterol, glucose tolerance, and serum uric acid in the random samples were also comparable to those of contemporary men nationwide (2).

FINDINGS

1. «Sudden Deaths», «Arrhythmic Deaths», and «Deaths in Circulatory Failure».

In the nationwide survey information was obtained sufficient to determine the duration of the final acute illness of 1476 (80.3 %) of 1839 deaths attributed to coronary heart disease. Sixty and four-tenths percent of these lasted less than one hour. These were classified as «sudden deaths». Forty-two and five-

tenths percent of the sudden deaths occurred in men who had not previously been known to have coronary heart disease.

Based on information from witnesses, rescue squads, physicians, hospitals, autopsies (31%), ECGs and ECG recordings at or shortly after the time of collapse (20.4%), and our own previous examinations, 141 of the 142 deaths among men who were intensively observed could be classified into two major categories (3) (Table 1). In 82 cases (58 %) the pulse ceased abruptly without prior collapse of the circulation and did not return spontaneously. The adequacy of the circulation for perfusing the brain immediately before death was indicated by the fact that the subjects were conscious (often active) or asleep and readily aroused. ECGs obtained at or shortly after the time of collapse showed ventricular fibrillation or asystole. These deaths were classified as «arrhythmic». In 59 cases (42 %) the peripheral circulation collapsed gradually, though sometimes rapidly, the subject lost consciousness and was not arousable, and the blood pressure could no longer be obtained, before the pulse finally ceased. These were classified as «deaths in circulatory failure».

The primary cause of «sudden death» in these men was the sudden development of a cardiac arrhythmia. All «instantaneous deaths» that occurred in less than five minutes were «arrhythmic». Ninety-one and three-tenths percent of deaths in less than one hour were «arrhythmic», 84.8 % of deaths in less than 24 hours were «arrhythmic», and 23.8 % of deaths in which the final illness lasted more than 24 hours were «arrhythmic».

Table 1. 142 deaths among 1020 men aged 40–65 observed five years prospectively

	Random Samples n = 687	High Risk Sample n = 333
All Deaths	72	70
Arrhythmic Deaths	40	42
Witnessed Directly	33	28
Not Witnessed Directly	7	14
Deaths in Circulatory Failure	31	28
Witnessed Directly	25	24
Not Witnessed Directly	6	4
Not Classifiable	1	0

*Table 2. Random Samples*  
Chronic myocardial disease present prior to death

	Arrhythmic Deaths n = 40 %	Circ. Fail. Deaths n = 31 %	P
1. Chronic Ischemic Mycardiopathy			
Symptomatic Ischemic Heart Disease	72.5	25.8	<.01
«Definite»*	62.5	16.1	
«Probable»*	10.0	9.7	
Old MI or Fibrosis	40.0	26.6	<.05
Occlusive Arteriosclerosis of Major Coronary Vessels	70.0	26.6	
2. LVH Patterns Present on ECG	40.0	12.9	
«Definite» or «Probable»*	25.0	0.0	<.05
«Possible»*	15.0	12.9	
3. Weight of Heart $\geq$ 400 Gms	80.0	46.7	NS
4. Cardiac Dilatation on X-Ray*	22.5	12.9	NS
5. Clinical Evidence of Chronic Congestive Heart Failure	45.0	29.0	NS
Disabling, Wholly or Partly	22.5	6.4	
Compensated, Not Disabling	22.5	22.5	
Any Clinical Evidence of Chronic Myocardial Disease	92.5	51.6	<.001
Four Manifestations	15.0	0.0	
Three Manifestations	7.5	3.2	
Two Manifestations	32.5	22.5	
One Manifestation	37.5	25.8	
No Clinical Evidence of Myocardial Disease	7.5	48.4	

\* For criteria, see references 13 and 14.

+ Observed transverse diameter  $\geq$  2 S.D. above expected for height and weight, or cardio-thoracic ratio  $\geq$  50 %, see references 2 and 15.

Probabilities based on Chi square.

## 2. Chronic Myocardial Disease Present Prior to Death

At the last examination prior to arrhythmic death, 92.5 % of men in the random samples had clinically detectable chronic myocardial disease (Table 2). Seventy-two and five-tenths percent had symptomatic or clinically evident chronic ischemic heart disease, 40 % had LVH patterns on the ECG, 22.5 % had cardiac dilatation in chest x-ray, and 45 % had evidence of chronic congestive heart failure. At autopsy, myocardial hypertrophy (80.0 %) was more frequent than occlusive coronary arteriosclerosis (70.0 %).

In the random samples 51.6 % of men who subsequently died in circulatory failure also had clinically detectable myocardial disease. However, the number of men with manifestations in each category was smaller, fewer men had multiple manifestations, and a significantly larger proportion (48.4 %) had no manifestations.

**Table 3. Random Samples**  
**Acute Myocardial Disorders Present at Time of Death**

	Arrhythmic Deaths n = 40 %	Circ. Fail. Deaths n = 31 %	P
1. Acute Ischemic Heart Disease	60.0	3.2	<.001
Symptomatic Acute IHD	35.3	3.2	
Definite Acute MI	14.7	3.2	
Acute CI or Probable Acute MI	20.6	0.0	
Asymptomatic Acute IHD (Acute MI or CO, autopsy)	22.5	0.0	
2. Exacerbation of Chronic Congestive Heart Failure	10.0	68.0	<.001
Acute	0.0	8.0	
Sub-Acute	10.0	60.0	
Moderate	2.5	0.0	
Moderately Severe	5.0	48.0	
Severe	2.5	26.0	
3. Clinical Evidence of Shock	10.0	100.0	<.001
Slight	2.5	0.0	
Moderate	5.0	0.0	
Moderately Severe	2.5	0.0	
Severe	0.0	100.0	
4. Evidence of Myocardial Anoxemia	25.0	100.0	<.001
Anoxic	22.5	48.0	
Moderately Severe	7.5	20.0	
Severe	15.0	28.0	
Anemic	2.5	100.0	
Any Clinical Evidence of Acute Myocardial Disorder	62.5	100.0	<.001

### 3. Acute Myocardial Disorders at the Time of Death

In the random samples, 62.5 % of men who experienced arrhythmic deaths, and 100 % of men who died in circulatory failure, had developed clinical evidence of acute abnormal conditions affecting the myocardium over a period of hours, days, or weeks immediately prior to death. The manifestations that preceded the two kinds of deaths were quite different (Table 3).

Sixty percent of men who experienced arrhythmic death had acute ischemic heart disease at the time of death. This was symptomatic in 35.3 % of the cases and was «silent» (not reported by the subject and not suspected by his associates) in 22.5 % of cases. In the «silent» cases it was represented by a recent acute myocardial infarction or coronary thrombosis discovered at autopsy. Only 3.2% of deaths in circulatory failure had symptomatic acute ischemic heart disease

and no «silent» acute lesions were found at autopsy.

Ten percent of men who experienced arrhythmic deaths experienced prior exacerbations of chronic congestive heart failure which was sub-acute in all cases, and clinically «severe» (disabling) in only 2.5 % of cases. Evidence of peripheral circulatory failure (shock) was present in only 10 % of arrhythmic deaths and was not severe in any case. On the other hand, 68 % of deaths in circulatory failure were preceded by exacerbations of congestive heart failure, of which 8 % were acute and 26 % severe; and 100 % of these deaths occurred in the setting of severe shock.

Evidence of acute anoxemia affecting the myocardium and arising from causes other than ischemic heart disease, was present at the time of death in 25 % of arrhythmic deaths. This was anoxic in 22.5 % of cases, and was caused primarily by acute exacerbations of severe, chronic obstructive pulmonary disease. Ane-

Table 4. Random Samples

Chronic Disorders of Heart Rate, Rhythm, Conduction And Repolarization Present Prior to Death

	Arrhythmic Deaths n = 40 %	Circ. Fail. Deaths n = 31 %	P
1. Disorders of Heart Rate	30.7	3.2	<.01
Sustained Tachycardia	20.5	3.2	<.05
Sustained Bradycardia	10.2	0.0	
2. Disorders of Pacemaker	37.5	12.9	<.05
Atrial Fibrillation	12.5	3.2	
Ectopic or Shifting Atrial Rhythm	22.5	9.6	
AV Junctional Rhythm	2.5	0.0	
Sinus Delay	15.8	0.0	.05
3. Supraventricular Dysrhythmias			
Supraventricular Premature Complexes			
SPCs $\geq$ 10/1000, PAT or MSPCs*	25.7	29.0	NS
4. QRS Duration $\geq$ .11 seconds	28.2	9.7	.05
5. Ventricular Dysrhythmias			
VPCs $\geq$ 10/1000	35.9	19.4	NS
Q form VPCs	43.6	23.3	<.1
Two or more forms of VPCs	51.2	36.7	NS
VPC Pairs	15.3	10.0	NS
Paroxysmal Ventricular Rhythms	5.1	3.3	NS
Early Cycle VPCs RR'/QT < 1	23.1	0.0	<.01
One or more of the above	71.8	41.9	<.02
6. QTc (Bazett) $\geq$ 440 msec	17.9	15.4	NS
None of the above abnormalities of rate, rhythm, conduction, or repolarization	7.5	48.4	<.001

\* Paroxysmal atrial tachycardia or multiple consecutive SPCs

mic anoxemia, associated with chronic anemias with hematocrit equal to or less than 15 %, was present in 2.5 % of cases. Anoxic anoxemia, caused by central respiratory failure from stroke or brain tumor, and by obstructive respiratory failure from carcinoma of the lung, pneumonia, congestive heart failure, and acute airway disease was present at the time of death in 48% of deaths in circulatory failure. All of the hearts of men who died in circulatory failure were considered to have had anemic anoxemia as a result of the profound circulatory collapse that was present at the time that the ventricular contractions ceased.

A larger proportion of the men who experienced arrhythmic deaths (57.5 % as contrasted with 25.8 %,  $P<.01$ ) were receiving medications with cardiac effects (digitalis glycosides, quinidine, other anti-

arrhythmic medications, vaso-dilators, anti-hypertensives, or diuretics) before the onset of their terminal illnesses. The only single category of medications in which there was a significant difference was digitalis glycosides (30.0 % vs 9.7 %,  $P<.05$ ).

Uremia (blood urea nitrogen up to 41 mg/dl) was present prior to 5 % of the arrhythmic deaths. Severe metabolic derangements were a feature of many of the terminal illnesses that preceded death in circulatory failure.

**Table 5. High Risk Sample**  
**Chronic Disorders of Heart Rate, Rhythm, Conduction, and Repolarization Present Prior to Death**

	Arrhythmic Deaths n = 42 %	Circ. Fail. Deaths n = 28 %	P
1. Disorders of Heart Rate	10.0	10.7	NS
Sustained Tachycardia	10.0	7.1	
Sustained Bradycardia	0.0	3.6	
2. Disorders of Pacemaker	16.7	14.2	NS
Atrial Fibrillation	2.4	3.6	
Ectopic or Shifting Atrial Rhythms	14.2	7.1	
AV Junctional Rhythms	2.4	3.6	
Sinus Delay	28.2	0.0	<.01
3. Supraventricular Dysrhythmias (SPCs $\geq$ 10/1000, PAT or MSPCs)	50.0	33.3	<.05
4. QRS Duration $\geq$ .11 Sec	35.7	35.7	NS
5. Ventricular Dysrhythmias			
VPC $\geq$ 10/1000	33.3	33.3	NS
Q Form VPCs	60.5	60.0	NS
Two or More Forms of VPCs	63.2	76.0	NS
VPC Pairs	31.5	20.0	NS
Paroxysmal Ventricular Rhythms	23.6	12.0	NS
Early Cycle VPCs RR'/QT <1	31.5	24.0	NS
One or more of the above	74.3	76.9	NS
6. QT <sub>c</sub> (Bazett) $\geq$ 440 msec	21.4	40.7	<.1
None of the above abnormalities of rate, rhythm, conduction, or repolarization	7.3	6.5	NS

#### *4. Chronic Disorders of Rate, Rhythm, Conduction and Repolarization Prior to Death*

In the random samples, 92.5 % of men who experienced arrhythmic death had prior chronic disorders of heart rate, rhythm, conduction or repolarization, and 51.6 % of men who died in circulatory failure had similar abnormalities (Table 4). In every category except supraventricular dysrhythmias and repolarization, the abnormalities were significantly more frequent among men who died arrhythmic deaths. The single abnormalities that most significantly distinguished between the two kinds of subsequent death were early cycle VPCs ( $P<.01$ ), sustained tachycardia ( $P<.05$ ), episodes of sinus delay ( $P<.05$ ), and «Q form» VPCs ( $P<.1$ ) in that order.

In the high risk sample, for which the men were selected partly on the basis of pre-existing disorders of rhythm and conduction, the only one of these variables that distinguished between arrhythmic death and death in circulatory failure at the last examination prior to death was sinus delay ( $P<.01$ ) (Table 5). There was no overall difference with respect to the prevalence of all other variables. Although a greater proportion of the men with arrhythmic death had preceding supraventricular dysrhythmias there was no significant difference between them and the deaths in circulatory failure with regard to any single kind of supraventricular dysrhythmia. A relatively larger proportion of the men who died in circulatory failure had evidence of prolonged repolarization shortly before death ( $P<.1$ ).

### 5. Central Nervous System Arousal, Position and Activity of the Subjects Immediately Prior to Death

With the exception of those who were under anaesthesia at the time of death, all of the men in these samples who experienced arrhythmic death were awake or asleep and arousable immediately before they collapsed and their ventricular contractions ceased, whereas all of the men who died in circulatory failure were comatose and not arousable. Sixty-six and five-tenths percent of men who experienced arrhythmic death were actively mobile, standing or sitting, at the time that they collapsed. All of the men who died in circulatory failure were lying immobile before their ventricular contractions ended (Table 6).

### 6. Precipitating Events

In all of the samples, 17.1 % of the men who experienced arrhythmic death collapsed while engaged in activities that are known to be associated with vagal effects upon the heart, and have been reported to be associated with the onset of dysrhythmias (Table 7) (4-10). Thirty-four and one-tenth percent of the arrhythmic deaths occurred during, or immediately (<5 min) after the subject had been engaged in activities known to be associated with the occurrence of myocardial ischemia or with sympathetic effects upon the heart, such as tachycardia, or an increase in ventricular dysrhythmias. All of these activities also have been reported to be associated with the occurrence of fatal arrhythmias (11,12,13). Fourteen and six-tenths percent of arrhythmic deaths occurred within a period of a few minutes to not more than four hours after the onset of pain and other symptoms of acute myocardial ischemia.

In all of the samples, 86.5 % of the deaths in circulatory failure were precipitated by conditions that led steadily and promptly (within minutes, hours, or a few days) to collapse of the peripheral circulation, and 13.5 % of these deaths were precipitated by conditions that led promptly to myocardial failure.

### 7. Mechanism of the Fatal Arrhythmia

We have observed four mechanisms by which sudden fatal (or potentially fatal) ventricular arrhythmias have occurred to men without prior collapse of the circulation: 1) An early cycle VPC falling in the vulnerable period of repolarization and initiating ventricular fibrillation. This occurred immediately following physical activity which produced a sinus tachycardia of 165/min (12); 2) A marked widening of the QT interval during a symptomatic episode of

**Table 6. All Samples**  
State of Arousal, Position and Activity of Subject Immediately Prior to Death

	Arrhythmic Deaths n = 82 %	Circ. Fail. Deaths n = 59 %
State of Arousal		
1. Awake	87.8	0.0
Highly Alert or Aroused	11.2	
2. Asleep	8.5	0.0
3. Under Anesthesia	3.7	3.4
4. Comatose, not arousable	0.0	96.6
Position and Activity		
1. Actively Mobile	17.7	0.0
2. Standing	22.0	0.0
3. Sitting	26.8	0.0
4. Lying	34.1	100.0
Occasionally moving	30.5	0.0
Immobile	3.7	100.0

**Table 7. All Samples –**  
Arrhythmic Deaths Precipitating Events

	Deaths n = 82 %
1. Activities Associated with Vagal Effects on Heart	17.1
Urinating	8.5
Defecating	1.2
Lifting-Straining	3.7
Diving into Swimming Pool	1.2
Shaving Neck	1.2
Drinking Iced Tea	1.2
2. Activities Associated with Sympathetic Effects on Heart	34.1
Physical Exercise	20.7
During	7.3
Immediately after	13.4
Immediately After Emotional Arousal	3.7
Driving Automobile	6.1
Tracheal Intubation	3.7
3. Episodes of Acute Myocardial Ischemia Symptomatic at time of death	14.6
4. No Apparent Precipitating Event Detected	34.1

**Table 8. All Samples – Deaths in Circulatory Failure Precipitating Events**

	Deaths n = 59 %
1. Conditions Leading to Failure of Peripheral Circulation	86.5
Acute Hemorrhage	18.6
Generalized Infection	37.3
Trauma (including surgical operations)	3.3
Pulmonary Embolism	1.7
Central Respiratory Failure (stroke, hepatic coma, brain tumor)	18.6
Obstructive Respiratory Failure (acute obstructive pulmonary disease, Ca lung)	6.7
2. Conditions Leading to Myocardial Failure	13.5
Acute Myocardial Infarction	10.1
Acute Congestive Heart Failure	3.4

myocardial ischemia, with an early cycle R-on-T VPC initiating ventricular fibrillation; 3) The apparently spontaneous appearance of a ventricular escape rhythm after a long RR interval during a period of bradycardia with rapid degeneration of the rhythm to ventricular fibrillation. This occurred to a man with a recent acute myocardial infarction; 4) A very rapid supraventricular tachycardia occurring during sleep, leading directly to the initiation of a rapid ventricular rhythm terminating in ventricular fibrillation.

#### 8. Risk Factors for Arrhythmic Death in Five Years

The multivariate analyses of the findings at the initial examination in relation to the outcome variable «arrhythmic death in five years» have not been completed. Initial results of single variable analyses based on all of the 1020 men in the samples, indicate that the significant ( $P < .01$ ) risk factors for the occurrence of arrhythmic death in five years fall into three categories:

a) Evidence of chronic myocardial disease: «definite» ischemic heart disease (14); LVH patterns on the ECG (15); definite evidence of cardiac dilatation on x-ray (observed cardiac diameter  $\geq 116\%$  of predicted, or cardio-thoracic ratio  $\geq 50\%$  (2,16), and clinical evidence of chronic congestive heart failure.

b) Chronic disorders of heart rate, rhythm, conduction, and repolarization: atrial fibrillation or other

constant abnormality of the pacemaker; QRS duration  $\geq .11$  sec;  $QT_c$  (Bazett)  $\geq 440$  msec (17); VPCs  $\geq 10/1000$  complexes, «Q form» VPCs (vertically directed in frontal plane), and early cycle VPCs ( $RR/QT < 1$ ) (18).

c) Factors that increase the risk that new events of heart disease, dysrhythmias, or anoxemia will occur: evidences of arteriosclerosis of peripheral vessels (intermittent claudication, stroke); now smoking cigarettes; now consuming five or more alcoholic drinks per day; and chronic obstructive pulmonary disease with severe airway disease.

#### SUMMARY AND CONCLUSIONS

«Arrhythmic deaths» were the primary cause of sudden death in these random samples of middle-aged American men. Ninety-one percent of the deaths within one hour, and 85 % of the deaths within 24 hours, were precipitated by the sudden occurrence of a cardiac arrhythmia at a time when the peripheral circulation had not collapsed and was still adequate to support the function of the brain.

The great majority of the men who experienced arrhythmic deaths had pre-existing myocardial disease, but this was often asymptomatic. As the data from the nationwide survey had indicated, only 72 % of the men who died «arrhythmic deaths» had previous clinically evident coronary heart disease; but 92.5 % of them had been found at prior examination to have detectable clinical evidence of chronic myocardial disease, including LVH patterns on the electrocardiogram, cardiac dilatation on x-ray, and clinical evidence of chronic congestive heart failure. At autopsy hearts that were hypertrophied were as prevalent among these men (80 %) as occlusive lesions of one or more major coronary vessels (70 %).

One-half of the men in the random samples who died in circulatory failure, had chronic myocardial disease similar to that of the men who experienced arrhythmic deaths. In general, the myocardial disease among the men who died in circulatory failure was not so far advanced as that which was found in the arrhythmic deaths; nevertheless, some men with severe and far advanced chronic myocardial disease died in circulatory failure. This was seen also among the men in the high risk sample. On the other hand, there was only one man who did not have preceding chronic myocardial disease who experienced an arrhythmic death; all other such men died in circulatory failure.



The arrhythmic deaths and the deaths in circulatory failure were distinguished from each other by the acute myocardial conditions that were present at the time of death.

The majority of arrhythmic deaths occurred in a setting of acute ischemic heart disease, or of myocardial anoxemia from other causes. In the random samples, 60 % of the arrhythmic deaths occurred in the setting of an episode of acute ischemic heart disease, which was asymptomatic in 22.5 % of the cases, and took the form of a «silent» acute myocardial infarction or coronary occlusion found at autopsy. The proportion of «silent» myocardial infarctions in this series is like that which has been reported from Seattle and Miami (19,20). At least 25 % of the arrhythmic deaths occurred in a setting of acute myocardial anoxemia from causes other than ischemic heart disease – chiefly anoxic anoxemia caused by acute exacerbations of chronic obstructive pulmonary disease and, in a few cases, from anemic anoxemia resulting from severe chronic anemias.

Deaths from circulatory failure occurred in the setting of shock and acute congestive heart failure. Only 3.2 % of the deaths in circulatory failure in the random samples occurred in the setting of acute ischemic heart disease. All of these deaths occurred, rather, in the setting of profound circulatory collapse, and 68 % of them occurred also in the setting of acute or sub-acute and severe exacerbations of congestive heart failure. Anoxic anoxemia from a variety of causes was present prior to death in many of these cases; but the acute myocardial anoxemia and other metabolic abnormalities that undoubtedly affected the myocardium at the time of death appeared to be primarily the result of the failure of the general circulation.

The prognostic significance of abnormalities of heart rate, rhythm, conduction, and repolarization when they were observed at the initial examination indicated that their presence enhanced the probability that an arrhythmic death would occur within five years. However, the simple presence, absence, or frequency of such disorders at the last examination prior to death was not the final determinant of whether or not an arrhythmic death would occur. In the random samples, 92.5 % of the arrhythmic deaths were preceded by chronic disorders of heart rate, rhythm, conduction, or repolarization, but similar abnormalities were absent in 48.4% of the deaths in circulatory failure. In the random samples, a larger proportion of the arrhythmic deaths had significant

chronic ventricular dysrhythmias, sustained tachycardia or bradycardia, abnormal supraventricular rhythms, sinus delay, or prolonged QRS conduction; but in the «high risk» sample the deaths in circulatory failure exhibited all the kinds of chronic disorders of rhythm and conduction that were present prior to the arrhythmic deaths, and, in general, in equal prevalence.

The functional state of the central nervous system immediately prior to death was of great importance in determining the kind of death that would occur. Most of the arrhythmic deaths occurred in men who were awake, often active and aroused. These deaths were, in many cases, precipitated by activities or conditions known to be accompanied by autonomic nervous effects – vagal or sympathetic – on cardiac function. The acute fatal arrhythmias that we have observed to occur in such cases have been initiated by mechanisms that might readily be set in motion by the kind of neural stimulation or the acute myocardial ischemia that was present at the time of many of the arrhythmic deaths.

During deaths in circulatory failure, the ventricular contractions did not cease until after the subject had become unconscious and was not arousable. Conditions that led to these deaths were set in motion when the subject was conscious, by events that led to circulatory collapse and unconsciousness. When such an acute event – a major hemorrhage, trauma, or a stroke, for example – occurred to a man who had very severe – even acute – myocardial disease accompanied by major abnormalities of rhythm or conduction, and who might therefore have been expected to experience an arrhythmic death, the result was not an arrhythmic death but a death in circulatory failure. This was true in all cases except in those in which the subject was under anaesthesia and an acute arrhythmia was precipitated by tracheal intubation.

The importance of the precipitating event in determining the nature of the fatal outcome places serious limits upon the extent to which the occurrence of an arrhythmic death can be predicted in advance from information based only upon features of the subject or his activities five years before the event.

In the estimation of risk of arrhythmic death within the next five years, the primary consideration lies in the evaluation of the amount and kind of myocardial disease now present, and in the presence or absence of disorders of heart rate, rhythm, conduction, or repolarization. The presence of the two kinds of variables together enhances the risk. Significant

disorders of heart rate, rhythm, or conduction appear to carry far less risk in the absence of significant myocardial disease than in its presence.

In the estimation of risk, consideration must also be given to the progressive nature of the underlying conditions that lead to the occurrence of arrhythmic death, and to the presence or absence of factors that influence the course of these conditions. The factors other than cardiac that most greatly affect the risk appear to be those that are most immediately related to the presence of the underlying heart disease or to the precipitation of the new acute conditions under which arrhythmic deaths occur: evidence of arteriosclerosis of vessels outside the heart; present cigarette smoking; high levels of alcohol intake; and the presence of severe airway disease carrying with it the risk of episodes of severe obstructive anoxemia. In the estimation of risk of death within five years, variables of this sort appear to carry with them much greater weight than the traditional «risk factors» such as high levels of serum cholesterol, elevated blood pressure, diabetes mellitus or high levels of serum uric acid, which, in younger people, are related to the development of coronary arteriosclerosis and to the occurrence of myocardial infarction.

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